

1

RECEIVED

DEC 2 3 2002

TECH CENTER 1600/2900

SEQUENCE LISTING

<110> GROLL, MICHAEL HUBER, ROBERT DITZEH, LARS ENGH, RICHARD

<120> PROCESS FOR THE PURIFICATION AND CRYSTALLIZATION OF PROTEASOME

<130> 100564-09039

<140> 09/381,286

<141> 1999-12-07

<150> PCT/EP98/01653

<151> 1998-03-20

<150> EPO 97104877.2

<151> 1997-03-21

<160> 14

<170> PatentIn Ver. 2.1

<210> 1

<211> 203

<212> PRT

<213> Thermoplasma acidophilum

<400> 1

Thr Thr Thr Val Gly Ile Thr Leu Lys Asp Ala Val Ile Met Ala Thr 1 5 10 15

Glu Arg Arg Val Thr Met Glu Asn Phe Ile Met His Lys Asn Gly Lys 20 25 30

Lys Leu Phe Gln Ile Asp Thr Tyr Thr Gly Met Thr Ile Ala Gly Leu 35 40 45

Val Gly Asp Ala Gln Val Leu Val Arg Tyr Met Lys Ala Glu Leu Glu
50 55 60

Leu Tyr Arg Leu Gln Arg Arg Val Asn Met Pro Ile Glu Ala Val Ala 65 70 75 80

Thr Leu Leu Ser Asn Met Leu Asn Gln Val Lys Tyr Met Pro Tyr Met 85 90 95

Val Gln Leu Val Gly Gly Ile Asp Thr Ala Pro His Val Phe Ser

Ile Asp Ala Ala Gly Gly Ser Val Glu Asp Ile Tyr Ala Ser Thr Gly
115 120 125

Ser Gly Ser Pro Phe Val Tyr Gly Val Leu Glu Ser Gln Tyr Ser Glu 130 135 140 Lys Met Thr Val Asp Glu Gly Val Asp Leu Val Ile Arg Ala Ile Ser 145 150 155 160

Ala Ala Lys Gln Arg Asp Ser Ala Ser Gly Gly Met Ile Asp Val Ala 165 170 175

Val Ile Thr Arg Lys Asp Gly Tyr Val Gln Leu Pro Thr Asp Gln Ile 180 185 190

Glu Ser Arg Ile Arg Lys Leu Gly Leu Ile Leu 195 200

<210> 2

<211> 205

<212> PRT

<213> Saccharomyces cerevisiae

<400> 2

Met Ser Asp Pro Ser Ser Ile Asn Gly Gly Ile Val Val Ala Met Thr 1 5 10 15

Gly Lys Asp Cys Val Ala Ile Ala Cys Asp Leu Arg Leu Gly Ser Gln
20 25 , 30

Ser Leu Gly Val Ser Asn Lys Phe Glu Lys Ile Phe His Tyr Gly His 35 40 45

Val Phe Leu Gly Ile Thr Gly Leu Ala Thr Asp Val Thr Thr Leu Asn 50 55 60

Glu Met Phe Arg Tyr Lys Thr Asn Leu Tyr Lys Leu Lys Glu Glu Arg
65 70 75 80

Ala Ile Glu Pro Glu Thr Phe Thr Gln Leu Val Ser Ser Ser Leu Tyr 85 90 95

Glu Arg Arg Phe Gly Pro Tyr Phe Val Gly Pro Val Val Ala Gly Ile 100 105 110

Asn Ser Lys Ser Gly Lys Pro Phe Ile Ala Gly Phe Asp Leu Ile Gly 115 120 125

Cys Ile Asp Glu Ala Lys Asp Phe Ile Val Ser Gly Thr Ala Ser Asp 130 135 140

Gln Leu Phe Gly Met Cys Glu Ser Leu Tyr Glu Pro Asn Leu Glu Pro 145 150 155 160

Glu Asp Leu Phe Glu Thr Ile Ser Gln Ala Leu Leu Asn Ala Ala Asp 165 170 175

Arg Asp Ala Leu Ser Gly Trp Gly Ala Val Val Tyr Ile Ile Lys Lys 180 185 190

Asp Glu Val Val Lys Arg Tyr Leu Lys Met Arg Gln Asp 195 200 205 <210> 3

<211> 198

<212> PRT

<213> Saccharomyces cerevisiae

<400> 3

Met Asp Ile Ile Leu Gly Ile Arg Val Gln Asp Ser Val Ile Leu Ala 1 5 10 15

Ser Ser Lys Ala Val Thr Arg Gly Ile Ser Val Leu Lys Asp Ser Asp 20 25 30

Asp Lys Thr Arg Gln Leu Ser Pro His Thr Leu Met Ser Phe Ala Gly 35 40 45

Glu Ala Gly Asp Thr Val Gln Phe Ala Glu Tyr Ile Gln Ala Asn Ile 50 55 60

Gln Leu Tyr Ser Ile Arg Glu Asp Tyr Glu Leu Ser Pro Gln Ala Val 65 70 75 80

Ser Ser Phe Val Arg Gln Glu Leu Ala Lys Ser Ile Arg Ser Arg Arg 85 90 95

Pro Tyr Gln Val Asn Val Leu Ile Gly Gly Tyr Asp Lys Lys Asn 100 105 110

Lys Pro Glu Leu Tyr Gln Ile Asp Tyr Leu Gly Thr Lys Val Glu Leu 115 120 125

Pro Tyr Gly Ala His Gly Tyr Ser Gly Phe Tyr Thr Phe Ser Leu Leu 130 135 140

Asp His His Tyr Arg Pro Asp Met Thr Thr Glu Glu Gly Leu Asp Leu 145 150 155 160

Leu Lys Leu Cys Val Gln Glu Leu Glu Lys Arg Met Pro Met Asp Phe 165 170 175

Lys Gly Val Ile Val Lys Ile Val Asp Lys Asp Gly Ile Arg Gln Val 180 185 190

Asp Asp Phe Gln Ala Gln 195

<210> 4

<211> 222

<212> PRT

<213> Saccharomyces cerevisiae

<400> 4

Gln Phe Asn Pro Tyr Gly Asp Asn Gly Gly Thr Ile Leu Gly Ile Ala 1 5 10

Gly Glu Asp Phe Ala Val Leu Ala Gly Asp Thr Arg Asn Ile Thr Asp
20 25 30

Tyr Ser Ile Asn Ser Arg Tyr Glu Pro Lys Val Phe Asp Cys Gly Asp 35 40 45

Asn Ile Val Met Ser Ala Asn Gly Phe Ala Ala Asp Gly Asp Ala Leu 50 55 60

Val Lys Arg Phe Lys Asn Ser Val Lys Trp Tyr His Phe Asp His Asn 65 70 75 80

Asp Lys Lys Leu Ser Ile Asn Ser Ala Ala Arg Asn Ile Gln His Leu 85 90 95

Leu Tyr Gly Lys Arg Phe Phe Pro Tyr Tyr Val His Thr Ile Ile Ala
100 105 110

Gly Leu Asp Glu Asp Gly Lys Gly Ala Val Tyr Ser Phe Asp Pro Val 115 120 125

Gly Ser Tyr Glu Arg Glu Gln Cys Arg Ala Gly Gly Ala Ala Ala Ser 130 135 140

Leu Ile Met Pro Phe Leu Asp Asn Gln Val Asn Phe Lys Asn Gln Tyr 145 150 155 160

Glu Pro Gly Thr Asn Gly Lys Val Lys Lys Pro Leu Lys Tyr Leu Ser 165 170 175

Val Glu Glu Val Ile Lys Leu Val Arg Asp Ser Phe Thr Ser Ala Thr 180 185 190

Glu Arg His Ile Gln Val Gly Asp Gly Leu Glu Ile Leu Ile Val Thr 195 200 205

Lys Asp Gly Val Arg Lys Glu Phe Tyr Glu Leu Lys Arg Asp 210 215 220

<210> 5

<211> 233

<212> PRT

<213> Saccharomyces cerevisiae

<400> 5

Thr Gln Gln Pro Ile Val Thr Gly Thr Ser Val Ile Ser Met Lys Tyr
1 5 10 15

Asp Asn Gly Val Ile Ile Ala Ala Asp Asn Leu Gly Ser Tyr Gly Ser
20 25 30

Leu Leu Arg Phe Asn Gly Val Glu Arg Leu Ile Pro Val Gly Asp Asn 35 40 45

Thr Val Val Gly Ile Ser Gly Asp Ile Ser Asp Met Gln His Ile Glu 50 55 60

Arg Leu Leu Lys Asp Leu Val Thr Glu Asn Ala Tyr Asp Asn Pro Leu 65 70 75 80 Ala Asp Ala Glu Glu Ala Leu Glu Pro Ser Tyr Ile Phe Glu Tyr Leu 85 90 95

Ala Thr Val Met Tyr Gln Arg Arg Ser Lys Met Asn Pro Leu Trp Asn 100 105 110

Ala Ile Ile Val Ala Gly Val Gln Ser Asn Gly Asp Gln Phe Leu Arg
115 120 125

Tyr Val Asn Leu Leu Gly Val Thr Tyr Ser Ser Pro Thr Leu Ala Thr 130 135 140

Gly Phe Gly Ala His Met Ala Asn Pro Leu Leu Arg Lys Val Val Asp 145 150 155 160

Arg Glu Ser Asp Ile Pro Lys Thr Thr Val Gln Val Ala Glu Glu Ala 165 170 175

Ile Val Asn Ala Met Arg Val Leu Tyr Tyr Arg Asp Ala Arg Ser Ser 180 185 190

Arg Asn Phe Ser Leu Ala Ile Ile Asp Lys Asn Thr Gly Leu Thr Phe 195 200 205

Lys Lys Asn Leu Gln Val Glu Asn Met Lys Trp Asp Phe Ala Lys Asp 210 215 220

Ile Lys Gly Tyr Gly Thr Gln Lys Ile 225 230

<210> 6

<211> 232

<212> PRT

<213> Saccharomyces cerevisiae

<400> 6

Thr Thr Ile Val Gly Val Lys Phe Asn Asn Gly Val Val Ile Ala Ala 1 5 10 15

Asp Thr Arg Ser Thr Gln Gly Pro Ile Val Ala Asp Lys Asn Cys Ala
20 25 30

Lys Leu His Arg Ile Ser Pro Lys Ile Trp Cys Ala Gly Ala Gly Thr 35 40 45

Ala Ala Asp Thr Glu Ala Val Thr Gln Leu Ile Gly Ser Asn Ile Glu 50 55 60

Leu His Ser Leu Tyr Thr Ser Arg Glu Pro Arg Val Val Ser Ala Leu 65 70 75 80

Gln Met Leu Lys Gln His Leu Phe Lys Tyr Gln Gly His Ile Gly Ala 85 90 95

Tyr Leu Ile Val Ala Gly Val Asp Pro Thr Gly Ser His Leu Phe Ser 100 105 110 Ile His Ala His Gly Ser Thr Asp Val Gly Tyr Tyr Leu Ser Leu Gly 115 120 125

Ser Gly Ser Leu Ala Ala Met Ala Val Leu Glu Ser His Trp Lys Gln 130 135 140

Asp Leu Thr Lys Glu Glu Ala Ile Lys Leu Ala Ser Asp Ala Ile Gln 145 150 155 160

Ala Gly Ile Trp Asn Asp Leu Gly Ser Gly Ser Asn Val Asp Val Cys
165 170 175

Val Met Glu Ile Gly Lys Asp Ala Glu Tyr Leu Arg Asn Tyr Leu Thr 180 185 190

Pro Asn Val Arg Glu Glu Lys Gln Lys Ser Tyr Lys Phe Pro Arg Gly 195 200 205

Thr Thr Ala Val Leu Lys Glu Ser Ile Val Asn Ile Cys Asp Ile Gln 210 215 220

Glu Glu Gln Val Asp Ile Thr Ala 225 230

<210> 7

<211> 234

<212> PRT

<213> Homo sapiens

<400> 7

Thr Thr Ile Ala Gly Leu Val Phe Gln Asp Gly Val Ile Leu Gly Ala
1 5 10 15

Asp Thr Arg Ala Thr Asn Asp Ser Val Val Ala Asp Lys Ser Cys Glu 20 25 30

Lys Ile His Phe Ile Ala Pro Lys Ile Tyr Cys Cys Gly Ala Gly Val 35 40 45

Ala Ala Asp Ala Glu Met Thr Thr Arg Met Val Ala Ser Lys Met Glu 50 60

Leu His Ala Leu Ser Thr Gly Arg Glu Pro Arg Val Ala Thr Val Thr 65 70 75 80

Arg Ile Leu Arg Gln Thr Leu Phe Arg Tyr Gln Gly His Val Gly Ala 85 90 95

Ser Leu Ile Val Gly Gly Val Asp Leu Thr Gly Pro Gln Leu Tyr Gly
100 105 110

Val His Pro His Gly Ser Tyr Ser Arg Leu Pro Phe Thr Ala Leu Gly 115 120 125

Ser Gly Gln Asp Ala Ala Leu Ala Val Leu Glu Asp Arg Phe Gln Pro 130 135 140 Asn Met Thr Leu Glu Ala Ala Gln Gly Leu Leu Val Glu Ala Val Thr 145 150 155 160

Ala Gly Ile Leu Gly Asp Leu Gly Ser Gly Gly Asn Val Asp Ala Cys 165 170 175

Val Ile Thr Lys Thr Gly Ala Lys Leu Leu Arg Thr Leu Ser Ser Pro 180 185 190

Thr Glu Pro Val Lys Arg Ser Gly Arg Tyr His Phe Val Pro Gly Thr 195 200 205

Thr Ala Val Leu Thr Gln Thr Val Lys Pro Leu Thr Leu Glu Leu Val 210 215 220

Glu Glu Thr Val Gln Ala Met Glu Val Glu 225 230

<210> 8

<211> 212

<212> PRT

<213> Saccharomyces cerevisiae

<400> 8

Thr Thr Thr Leu Ala Phe Arg Phe Gln Gly Gly Ile Ile Val Ala Val

1 10 15

Asp Ser Arg Ala Thr Ala Gly Asn Trp Val Ala Ser Gln Thr Val Lys
20 25 30

Lys Val Ile Glu Ile Asn Pro Phe Leu Leu Gly Thr Met Ala Gly Gly 35 40 45

Ala Ala Asp Cys Gln Phe Trp Glu Thr Trp Leu Gly Ser Gln Cys Arg
50 55 60

Leu His Glu Leu Arg Glu Lys Glu Arg Ile Ser Val Ala Ala Ala Ser 65 70 75 80

Lys Ile Leu Ser Asn Leu Val Tyr Gln Tyr Lys Gly Ala Gly Leu Ser 85 90 95

Met Gly Thr Met Ile Cys Gly Tyr Thr Arg Lys Glu Gly Pro Thr Ile 100 105 110

Tyr Tyr Val Asp Ser Asp Gly Thr Arg Leu Lys Gly Asp Ile Phe Cys 115 120 125

Val Gly Ser Gly Gln Thr Phe Ala Tyr Gly Val Leu Asp Ser Asn Tyr 130 135 140

Lys Trp Asp Leu Ser Val Glu Asp Ala Leu Tyr Leu Gly Lys Arg Ser 145 150 155 160

Ile Leu Ala Ala Ala His Arg Asp Ala Tyr Ser Gly Gly Ser Val Asn 165 170 175 Leu Tyr His Val Thr Glu Asp Gly Trp Ile Tyr His Gly Asn His Asp 180 185 190

Val Gly Glu Leu Phe Trp Lys Val Lys Glu Glu Glu Gly Ser Phe Asn 195 200 205

Asn Val Ile Gly 210

<210> 9

<211> 204

<212> PRT

<213> Homo sapiens

<400> 9

Thr Thr Leu Ala Phe Lys Phe Arg His Gly Val Ile Val Ala Ala 1 5 10 15

Asp Ser Arg Ala Thr Ala Gly Ala Tyr Ile Ala Ser Gln Thr Val Lys
20 25 30

Lys Val Ile Glu Ile Asn Pro Tyr Leu Leu Gly Thr Met Ala Gly Gly 35 40 45

Ala Ala Asp Cys Ser Phe Trp Glu Arg Leu Leu Ala Arg Gln Cys Arg 50 55 60

Ile Tyr Glu Leu Arg Asn Lys Glu Arg Ile Ser Val Ala Ala Ala Ser
65 70 75 80

Lys Leu Leu Ala Asn Met Val Tyr Gln Tyr Lys Gly Met Gly Leu Ser 85 90 95

Met Gly Thr Met Ile Cys Gly Trp Asp Lys Arg Gly Pro Gly Leu Tyr
100 105 110

Tyr Val Asp Ser Glu Gly Asn Arg Ile Ser Gly Ala Thr Phe Ser Val 115 120 125

Gly Ser Gly Ser Val Tyr Ala Tyr Gly Val Met Asp Arg Gly Tyr Ser 130 135 140

Tyr Asp Leu Glu Val Glu Gln Ala Tyr Asp Leu Ala Arg Arg Ala Ile 145 150 155 160

Tyr Gln Ala Thr Tyr Arg Asp Ala Tyr Ser Gly Gly Ala Val Asn Leu 165 170 175

Tyr His Val Arg Glu Asp Gly Trp Ile Arg Val Ser Ser Asp Asn Val 180 185 190

Ala Asp Leu His Glu Lys Tyr Ser Gly Ser Thr Pro 195 200 <210> 10

<211> 204

<212> PRT

<213> Homo sapiens

<400> 10

Thr Thr Leu Ala Phe Lys Phe Gln His Gly Val Ile Ala Ala Val

1 5 10 15

Asp Ser Arg Ala Ser Ala Gly Ser Tyr Ile Ser Ala Leu Arg Val Asn 20 25 30

Lys Val Ile Glu Ile Asn Pro Tyr Leu Leu Gly Thr Met Ser Gly Cys 35 40 45

Ala Ala Asp Cys Gln Tyr Trp Glu Arg Leu Leu Ala Lys Glu Cys Arg
50 55 60

Leu Tyr Tyr Leu Arg Asn Gly Glu Arg Ile Ser Val Ser Ala Ala Ser 65 70 75 80

Lys Leu Leu Ser Asn Met Met Cys Gln Tyr Arg Gly Met Gly Leu Ser 85 90 95

Met Gly Ser Met Ile Cys Gly Trp Asp Lys Lys Gly Pro Gly Leu Tyr
100 105 110

Tyr Val Asp Glu His Gly Thr Arg Leu Ser Gly Asn Met Phe Ser Thr 115 120 125

Gly Ser Gly Asn Thr Tyr Ala Tyr Gly Val Met Asp Ser Gly Tyr Arg 130 135

Pro Asn Leu Ser Pro Glu Glu Ala Tyr Asp Leu Gly Arg Arg Ala Ile 145 . 150 . 155 . 160

Ala Tyr Ala Thr His Arg Asp Ser Tyr Ser Gly Gly Val Val Asn Met 165 170 175

Tyr His Met Lys Glu Asp Gly Trp Val Lys Val Glu Ser Thr Asp Val 180 185 190

Ser Asp Leu Leu His Gln Tyr Arg Glu Ala Asn Gln 195 200

<210> 11

<211> 196

<212> PRT

<213> Saccharomyces cerevisiae

<400> 11

Thr Ser Ile Met Ala Val Thr Phe Lys Asp Gly Val Ile Leu Gly Ala 1 5 10 15

Asp Ser Arg Thr Thr Gly Ala Tyr Ile Ala Asn Arg Val Thr Asp
20 25 30

Lys Leu Thr Arg Val His Asp Lys Ile Trp Cys Cys Arg Ser Gly Ser 35 40 45

Ala Ala Asp Thr Gln Ala Ile Ala Asp Ile Val Gln Tyr His Leu Glu 50 55 60

Leu Tyr Thr Ser Gln Tyr Gly Thr Pro Ser Thr Glu Thr Ala Ala Ser 65 70 75 80

Val Phe Lys Glu Leu Cys Tyr Glu Asn Lys Asp Asn Leu Thr Ala Gly 85 90 95

Ile Ile Val Ala Gly Tyr Asp Asp Lys Asn Lys Gly Glu Val Tyr Thr
100 105 110

Ile Pro Leu Gly Gly Ser Val His Lys Leu Pro Tyr Ala Ile Ala Gly 115 120 125

Ser Gly Ser Thr Phe Ile Tyr Gly Tyr Cys Asp Lys Asn Phe Arg Glu 130 135 140

Asn Met Ser Lys Glu Glu Thr Val Asp Phe Ile Lys His Ser Leu Ser 145 150 155 160

Gln Ala Ile Lys Trp Asp Gly Ser Ser Gly Gly Val Ile Arg Met Val
165 170 175

Val Leu Thr Ala Ala Gly Val Glu Arg Leu Ile Phe Tyr Pro Asp Glu
180 185 190

Tyr Glu Gln Leu 195

<210> 12

<211> 205

<212> PRT

<213> Homo sapiens

<400> 12

Thr Thr Ile Met Ala Val Gln Phe Asp Gly Gly Val Val Leu Gly Ala
1 5 10 15

Asp Ser Arg Thr Thr Gly Ser Tyr Ile Ala Asn Arg Val Thr Asp
20 25 30

Lys Leu Thr Pro Ile His Asp Arg Ile Phe Cys Cys Arg Ser Gly Ser 35 40 45

Ala Ala Asp Thr Gln Ala Val Ala Asp Ala Val Thr Tyr Gln Leu Gly 50 55

Phe His Ser Ile Glu Leu Asn Glu Pro Pro Leu Val His Thr Ala Ala 65 70 75 80

Ser Leu Phe Lys Glu Met Cys Tyr Arg Tyr Arg Glu Asp Leu Met Ala 85 90 95

Gly Ile Ile Ile Ala Gly Trp Asp Pro Gln Glu Gly Gly Gln Gly Tyr 100 105 110

Ser Val Pro Met Gly Gly Met Met Val Arg Gln Ser Phe Ala Ile Gly 115 120 125

Gly Ser Gly Ser Ser Tyr Ile Tyr Gly Tyr Val Asp Ala Thr Tyr Arg 130 135 140

Glu Gly Met Thr Lys Glu Glu Cys Leu Gln Phe Thr Ala Asn Ala Leu 145 150 155 160

Ala Leu Ala Met Glu Arg Asp Gly Ser Ser Gly Gly Val Ile Arg Leu 165 170 175

Ala Ala Ile Ala Glu Ser Gly Val Glu Arg Gln Val Leu Leu Gly Asp 180 185 190

Gln Ile Pro Lys Phe Ala Val Ala Thr Leu Pro Pro Ala 195 200 205

<210> 13

<211> 199

<212> PRT

<213> Homo sapiens

<400> 13

Thr Thr Ile Met Ala Val Glu Phe Asp Gly Gly Val Val Met Gly Ser 1 5 10 15

Asp Ser Arg Val Ser Ala Gly Glu Ala Val Val Asn Arg Val Phe Asp 20 25 30

Lys Leu Ser Pro Leu His Glu Arg Ile Tyr Cys Ala Leu Ser Gly Ser 35 40 45

Ala Ala Asp Ala Gln Ala Val Ala Asp Met Ala Ala Tyr Gln Leu Glu 50 55 60

Leu His Gly Ile Glu Leu Glu Glu Pro Pro Leu Val Leu Ala Ala 65 70 75 80

Asn Val Val Arg Asn Ile Ser Tyr Lys Tyr Arg Glu Asp Leu Ser Ala 85 90 95

His Leu Met Val Ala Gly Trp Asp Gln Arg Glu Gly Gly Gln Val Tyr 100 105 110

Gly Thr Leu Gly Gly Met Leu Thr Arg Gln Pro Phe Ala Ile Gly Gly
115 120 125

Ser Gly Ser Thr Phe Ile Tyr Gly Tyr Val Asp Ala Ala Tyr Lys Pro 130 135 140

Gly Met Ser Pro Glu Glu Cys Arg Arg Phe Thr Thr Asp Ala Ile Ala 145 150 155 160 Leu Ala Met Ser Arg Asp Gly Ser Ser Gly Gly Val Ile Tyr Leu Val
165 170 175

Thr Ile Thr Ala Ala Gly Val Asp His Arg Val Ile Leu Gly Asn Glu 180 185 190

Leu Pro Lys Phe Tyr Asp Glu 195

<210> 14

<211> 4

<212> PRT

<213> Thermoplasma acidophilum

<400> 14

Tyr Gly Gly Val

1